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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/608,354	06/27/2003	Stanley T. Crook	MSIBIS-0002USC2	2899
27180	7590	06/08/2010	EXAMINER	
ISIS PHARMACEUTICALS INC 1896 RUTHERFORD RD. CARLSBAD, CA 92008			LU, FRANK WEI MIN	
			ART UNIT	PAPER NUMBER
			1634	
			MAIL DATE	DELIVERY MODE
			06/08/2010	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/608,354	<b>Applicant(s)</b> CROOK ET AL.	
	<b>Examiner</b> FRANK W. LU	<b>Art Unit</b> 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 2/24/2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 38,39,95,97-99,101,103,104,109-112 and 115-120 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 38,39,95,97-99,101,103,104,109-112 and 115-120 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 03 January 2008 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Response to Amendment***

1. Applicant's response to the office action filed on February 24, 2010 has been entered. The claims pending in this application are claims 38, 39, 95, 97-99, 101, 103, 104, 109-112, and 115-120. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn in view of applicant's amendment filed on February 24, 2010.

### ***Claim Objections***

2. Claim 104 is objected to because of the following informality: "each test compound" is "the each test compound".
3. Claim 111 is objected to because of the following informality: "at least one test compound-nucleic acid target complex" in step (e) should be "said at least one test compound-nucleic acid target complex".
4. Claim 112 is objected to because of the following informality: "at least one test compound-nucleic acid target complex" in steps (f) to (h) should be "said at least one test compound-nucleic acid target complex".

Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. New Matter

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Claims 38, 39, 95, 97-99, 101, 103, 104, 109-112, and 115-120 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The limitations “the mass of the nucleic acid target is known” and “the mass of each test compound is known” is added to the newly amended independent claim 111 while the limitation “the mass of each test compound is known” is added to the newly amended independent claim 112. Although the specification describes a method for identifying in a combinatorial mixture compounds which bind to a biomolecular target, wherein the method comprises: (a) providing mass spectral data on the ion abundance for said biomolecular target; (b) providing a first complex of said biomolecular target and a standard binding compound which binds to said target; (c) combining with said first complex a combinatorial mixture of compounds; (d) ionizing in a mass spectrometer said combination from step (c) to provide a plurality of ions for said combination; (e) collecting from the ionization of step (d) mass spectral data on the ion abundance of said first complex, wherein said ion abundances in steps (a) and (e) affords information for effecting said determination wherein mass differences in the mass spectral data from steps (a) and (e) are identified for determining the mass of compounds from the combinatorial mixture which preferentially bind with said biomolecular target (e.g., see page 76, original filed claims 42 and 43), the specification fails to define or provide any disclosure to support such claim limitations recited in claims 111 and 112. Furthermore, nowhere in the specification describes the limitation “using the ion abundance data collected in step (e) to

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calculate the relative concentrations of the first complex and the at least one test compound-nucleic acid target complex” as recited in newly added claims 116 and 119. In addition, in applicant’s remarks filed on February 24, 2010, applicant does not indicate which parts in the specification support such claim limitations in claims 111, 112, 116, and 119.

MPEP 2163.06 notes “IF NEW MATTER IS ADDED TO THE CLAIMS, THE EXAMINER SHOULD REJECT THE CLAIMS UNDER 35 U.S.C. 112, FIRST PARAGRAPH - WRITTEN DESCRIPTION REQUIREMENT. *IN RE RASMUSSEN*, 650 F.2D 1212, 211 USPQ 323 (CCPA 1981).” MPEP 2163.02 teaches that “Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application.” MPEP 2163.06 further notes “WHEN AN AMENDMENT IS FILED IN REPLY TO AN OBJECTION OR REJECTION BASED ON 35 U.S.C. 112, FIRST PARAGRAPH, A STUDY OF THE ENTIRE APPLICATION IS OFTEN NECESSARY TO DETERMINE WHETHER OR NOT “NEW MATTER” IS INVOLVED. *APPLICANT SHOULD THEREFORE SPECIFICALLY POINT OUT THE SUPPORT FOR ANY AMENDMENTS MADE TO THE DISCLOSURE*” (emphasis added).

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 99, 101, 104, 110, 112, and 118-120 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claim 112 is rejected as vague and indefinite. Since the claim does not require that the mass of the target nucleic acid or the mass of the standard binding compound is known, if the mass of the first complex and the mass of the least one test compound-nucleic acid target complex are A and B respectively which are calculated from step (g), and the mass of the target nucleic acid, the mass of the standard binding compound, and the mass of the test compound in the least one test compound-nucleic acid target complex are unknown and are X, Y, and Z

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respectively, there are two equations as following:  $A=X+Y$  and  $B=X+Z$ . Since, from step (h), only mass difference between A and B can be calculated ( $A-B=Y-Z$  or  $B-A=Z-Y$ ) and the mass of the test compound in the least one test compound-nucleic acid target complex can not be calculated, it is unclear why the identity of the test compound bound in the at least one test compound-nucleic acid target complex can be determined by calculating the difference between the mass of the first complex and the at least one test compound-nucleic acid target complex as recited in step (h). Please clarify.

### ***Conclusion***

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. No claim is allowed.

12. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of

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such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746.

The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen, can be reached on (571)272-0731.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Frank W Lu /  
Primary Examiner, Art Unit 1634  
June 4, 2010